Remarks

The Applicants note with appreciation the rejoinder of Groups IV and VIII; Groups VI and IX; and Groups VII and X.

The disclosure stands objected to with respect to embedded hyperlinks. The Applicants have amended the Specification to remove such hyperlinks. The Applicants have further amended the Specification to correct several minor typographical errors and to place the Specification into final condition for allowance. Withdrawal of the objection is respectfully requested.

Claim 6 stands objected to over formalities concerning "matrices B, C of mutations." The Applicants have amended Claim 6 in accordance with the Examiner's helpful suggestion by utilizing "and" between B and C. Withdrawal of the objection is respectfully requested.

Claims 6 stands rejected under 35 U.S.C. §112, second paragraph as being indefinite. The Applicants note with appreciation the Examiner's helpful comments with respect to the five issues of concern with respect to Claim 6. The Applicants have amended Claim 6 to account for the omission of variable k. Thus, Claim 6 now recites that there is a numerical matrix of dimensions NxM and positions i, j or k. Claim 6 also recites that i, j and k are in pairs corresponding to a column number and a line number in the matrix. This utilization of variables i, j or k is a part of a well established general rule wherein the first letter (A, B or C) represents a matrix (A, B, or C) and the two following letters (i, j or k) correspond to the number of the columns and the number of the lines.

This is readily seen by reference to the Applicants' Specification. In that regard, A, B and C are matrices of sequences as exemplified in ¶ [0087] for matrix A, ¶ [0088] for matrix B and ¶ [0089] for matrix C. In matrix A, the columns correspond to the positions of a motif in a sequence and the lines correspond to the sequences. In matrix B and C, the lines and the columns correspond both to positions of motifs in the sequence. Therefore, $B_{i,k}$ represents the square located at the i column and the k line of matrix B. The value of i, j or k relates to the positions of the mutations in the sequence. Thus, the Applicants provide methods which can analyze a huge number of sequence because it seeks at least two non simultaneous mutations.

Thus, the Applicants respectfully submit that the variable k has been fully defined and that there is now antecedent basis for $A_{k,j}$; $C_{k,i}$; and $C_{i,k}$. The Applicants have also removed reference to "in which i j" in those claims. In light of the foregoing, the Applicants respectfully submit that Claim 6 is now definite. Withdrawal of the rejection is respectfully requested.

Claims 1-20, 28 and 29 stand rejected under 35 U.S.C. §101. The Applicants again note with appreciation the Examiner's helpful comments with respect to suggested amendments. The Applicants have accordingly amended Claim 1 to include a new step d) which recites outputting the identified motifs to at least one of a display, a memory, another computer, a network or a user, or physically transforming the identified motifs. Inasmuch as this is in accordance with the Examiner's suggested language, the Applicants respectfully submit that all of Claims 1-20, 28 and 29 are fully in compliance with §101. Withdrawal of the rejection is respectfully requested.

Claims 1-20, 28 and 29 stand rejected under 35 U.S.C. §112, first paragraph as not being enabled. The Applicants respectfully submit that all of those claims are in full compliance with §112, first paragraph for the reasons set forth below.

The Applicants first note with appreciation the Examiner's detailed comments with respect to the *In re Wands* test for enablement. In that regard, the Applicants agree that the skill of those in the art is high. However, although the claims are in some respects broad, "undue" experimentation would hardly be necessary. In fact, the experimentation necessary with respect to the solicited claims in no more than ordinary experimentation. It should be noted that routine experimentation oftentimes constitutes a large quantity of experimentation, so long as that experimentation is "undue".

Various articles have been employed in the rejection to demonstrate a lack of teaching with respect to certain methodology or algorithms. However, those selected articles are not necessarily illustrative of what is known to those skilled in the art. Thus, the Applicants note that step a) of Claim 1 can be performed with any aligning software such as HMMer or CLUSTAL which is suitable for the claimed subject matter in dealing with thousands of sequences in less than an hour. The Applicants respectfully submit that these are well known and available software programs and that use of such programs that can provide results for that step in less than an hour hardly constitute "undue" experimentation.

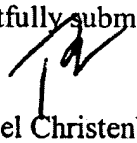
Step b) of Claim 1 relates to a classic comparison of sequences such as disclosed for the example in the Korber article cited in the rejection or in another article of Korber in *Proc. Natl. Acad. Sci. USA*, copy enclosed. Again, the Applicants respectfully submit that utilization of such a classic comparison of sequences is would hardly constitute the need for "undue" experimentation.

Step c) is an important step in the claimed method. It is clear that after the comparison of step b) that step c) relates to the identification of positions that have never simultaneously mutated or, to the contrary, that have simultaneously mutated and to assign a 0 or a 1 to those positions (Boolean state). The Applicants respectfully submit that step c) is also well within the purview of one skilled in the art which would again hardly constitute "undue" experimentation.

The Applicants have demonstrated that the individual steps do not involve undue experimentation. Moreover, the Applicants' Specification teaches those skilled in the art to employ those three steps in the prescribed manner as set forth in, for example, Claim 1. The result is that one skilled in the art would actually require comparatively little time and effort to practice the subject matter of the solicited claims. In any event, the time and effort required to successfully perform the claimed steps does not come even close to "undue" experimentation. Withdrawal of the rejection is respectfully requested.

In light of the foregoing, the Applicants respectfully submit that the entire Application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,



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